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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,983	01/04/2005	Yasuhiro Kajihara	ACT-001	3218

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OSHA LIANG L.L.P.
TWO HOUSTON CENTER
909 FANNIN, SUITE 3500
HOUSTON, TX 77010

EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
11/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@oshaliang.com
buta@oshaliang.com

Office Action Summary	Application No.	Applicant(s)	
	10/519,983	KAJIHARA, YASUHIRO	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

This Office Action is in response to Applicant's request for continued examination (RCE) filed September 17, 2009, and amendment and response to the Final Office Action (mailed June 17, 2009), filed September 17, 2009 wherein claims 1, 5-7, and 22-25 are amended.

Claims 1, 5-7, and 22-25 are pending and are examined on the merits herein.

The rejection of claims 1, 5-7, and 22-25 under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns in view of Komba and Ratcliffe is withdrawn in view of the amendment to claim 1 and the modified rejection set forth below.

It is noted that the order of steps 6-11 in claim 1 was modified to include the new step of preparing the asparagine-linked disialooligosaccharide, but the changes were not indicated by underlining new material and crossing through deleted material.

Claim Objections

Claims 1 , 5, and 6 are objected to because of the following informalities: In step (5) of claim 1, "lease" should be "least." Claim 5 recites "at least sugar residues," which

previously read "at least 6 sugar residues." Claim 6 recites "9 o 11 sugar residues," which should be "9 to 11 sugar residues." Appropriate correction is required.

The following are new or modified rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claim 1 and dependent claims 5-7 and 22-25 recite the limitation "under pH 5 to 6." This limitation could be interpreted to mean that the reaction occurs under the conditions of pH 5 to 6, or it could be interpreted to mean that the reaction occurs at a pH lower than 5 to 6. Thus, the scope of the claim is unclear.

Claim 5 requires "at least sugar residues." The previous claim set (April 7, 2009) read "at least 6 sugar residues." It is unclear if claim 5 only contains a typo and is intended to read "at least 6 sugar residues" or if claim 5 is intended to encompass any number of sugar residues.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the response submitted September 17, 2009, independent claim 1 was amended to require the preparation of a protected compound wherein the "benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under pH 5 to 6." Applicant states that support for this amendment can be found in paragraph [0141] of the published application. The limitation "under pH 5 to 6" is indefinite, as set forth above. However, if the limitation is intended to mean that the reaction is carried out at a pH lower than 5 to 6, the limitation introduces new matter because reaction at a pH lower than 5 to 6 is not described in the specification. Furthermore, although paragraph [0141] describes benzyl protection at pH 5 to 6, the examiner was unable to locate support for allyl or diphenylmethyl protection at pH 5-6. The examiner was unable to locate a general description of pH required for protection of sialic acid derivatives, and the recitation pH 5-6 in paragraph [0141] is given as part of the specific conditions used for benzyl protection. This is a new matter rejection.

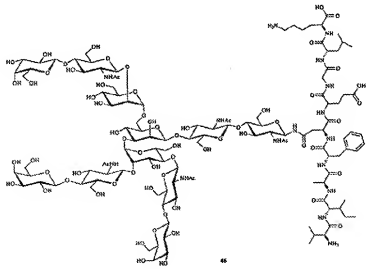
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) in view of Keil et al. (Angew. Chem. Int. Ed. 2001, 40, No.2, pp. 366-369) and Greene et al. (Protective Groups in Organic Synthesis, Third Edition, John Wiley & Sons, Inc., 1999, pages 415-419).

Meinojohanns teaches a method for preparing asparagine-linked glycopeptides such as the one shown below [page 556, Scheme 5]:

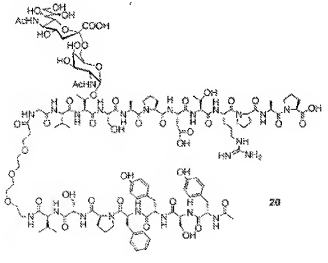


The products can be prepared by attaching an Fmoc-protected amino acid to a resin, followed by deprotection of the Fmoc group and coupling of another amino acid,

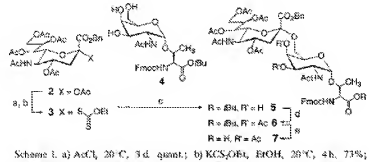
which is repeated. Then the asparagine building blocks, which are protected with Fmoc as well (see page 555, Scheme 4), are coupled and the peptide synthesis is continued as described above. Both di- and tri-antennary building blocks are taught [page 555, Scheme 4]. Finally, the glycopeptide is cleaved from the resin. [pages 559-560]. Secreted and cell-surface proteins are glycosylated with both N- and O-linked oligosaccharides, and the effects of the sugars on such properties as immunogenicity is of importance [page 549, first paragraph]. The N-linked glycopeptides prepared by Meinojohanns could be used as substrates for 1-6-sialyltransferase [page 556, scheme 5].

The difference between Meinojohanns' process and the claimed process is that Meinojohanns does not utilize an asparagine building block which contains a sialic acid moiety, but instead suggests the use of sialyltransferase to introduce sialyl moieties into the product.

Keil teaches a process for preparing compound 20, which contains a sialic acid moiety [page 368, Scheme 4].



Compound 20 is prepared by a process which includes preparation of sialic acid-containing building block 7, shown below, which is then used in the solid-phase synthesis of the glycododecapeptide sequence of compound 20 [page 367, Scheme 1].



Scheme 1. a) $AcCl_3$, 20 °C, 3 d, quant.; b) KCS_2OEt, EtOH, 20 °C, 4 h, 73%; c) $CH_3SBr/AgOTf$, CH_3CN/CH_2Cl_2 (2/1), -62 °C, 3 h, 60%; d) Ac_2O, pyridine, 0 °C, 4 h, 84%; e) TFA/CH_2Cl_2 (1/1), anisole, 20 °C, 6 h, quant. Ac = acetyl, Tf = trifluoromethanesulfonyl, TFA = trifluoroacetic acid.

The carboxylic acid moiety of sialic acid-containing compounds 2-7 was protected as a benzyl ester, as shown above.

Greene teaches methods for protecting a carboxylic acid as its benzyl ester. In one example, a selective protection is carried out under acidic conditions [page 416, entry 5]. The carboxyl group which is near the amino group is left unprotected, while the other carboxyl group is protected.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out Meinojohanns' process for preparing glycopeptides, using an asparagine building block which contains sialic acid groups. The claimed invention can be seen as an improvement over Meinojohanns' method because the sialyl group is present without requiring addition enzymatic transformation. Keil teaches a method for preparing the sialic acid-containing building blocks, which are coupled to the peptide in the same way that Meinojohanns' building blocks are coupled. Thus, the

skilled artisan could prepare sialic acid-containing building blocks for use in Meinojohanns' process, and avoid additional enzymatic transformation. Keil's sialic acid is protected as the benzyl ester. Greene teaches a number of methods for protecting carboxylic acids as the benzyl ester, including one which is carried out under acidic conditions. Greene does not teach the exact pH required to achieve protection, but it is routine in the art for the skilled artisan to optimize reaction conditions for suitability to the particular substrate which is being protected. Thus, the claimed invention is obvious over Meinojohanns in view of Keil and Greene.

Response to Arguments

Applicant's arguments with respect to Komba and Ratcliffe are moot in view of the new ground of rejection.

Applicant argues that the carboxyl group of sialic acid can be selectively protected at pH 5 to 6. As set forth above, the carboxyl group of sialic acid has been protected as the benzyl ester in a prior art process for preparing glycopeptides. One method of benzyl protection occurs under acidic conditions. Thus, it would have been obvious to protect sialic acid as the benzyl ester and to use acidic conditions to do so. Furthermore, Greene teaches a benzyl protection which is carried out under acidic conditions which results in selective carboxyl group protection.

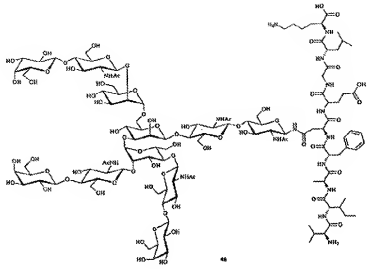
Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (Angew. Chem. 2003, 115, 2641-2644, published

online June 5, 2003) in view of Meinojohanns (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560, PTO-1449 submitted December 20, 2007).

Yamamoto teaches a solid-phase step-wise assembly of an N-linked sialylglycopeptide [page 2641, right column, fourth paragraph]. Fmoc-protected serine was coupled to PEGA resin, followed by amidation of another Fmoc-protected serine. The oligosaccharide was introduced through Fmoc-Asn-OH, and then the other amino acids were coupled as OPfp esters. After construction of the glycopeptides, the sialylglycopeptide was deprotected and cleaved from the resin. [page 2641, last paragraph – page 2642, first paragraph]. The disialyloligosaccharide was protected using Cs_2CO_3 and BnBr at pH 6 [page 2641, right column, third paragraph, and supporting information, page 2].

Yamamoto's process does not repeat claimed steps (3) and (4) because the target compound only requires two amino acid residues before the oligosaccharide is introduced. However, Yamamoto's procedure could be utilized for larger target compounds.

As set forth above, Meinojohanns teaches a similar solid-phase step-wise method for preparing asparagine-linked glycopeptides such as the one shown below [page 556, Scheme 5], which can be subjected to sialyltransferase [page 556, scheme 5] to obtain the sialylated product:



It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out to use Yamamoto's process for the preparation of larger glycopeptides such as the one taught by Meinojohanns, which would require repetition of steps 3 and 4. The skilled artisan would expect that Yamamoto's process could be utilized to achieve a sialylated analog of Meinojohanns' product because the coupling steps are done in the same way.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623